L19 ANSWER 1 OF 2 USPATFULL

ACCESSION NUMBER: 96:27183 USPATFULL
TITLE: Enteral nutritional composition having balanced amino acid profile
INVENTOR(S): Schmidl, Mary K., Arden Hills, MN, United States
Kvamme, Candis, Brooklyn Park, MN, United States
PATENT ASSIGNEE(S): Sandoz Nutrition Ltd., Berne, Switzerland (non-U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5504072	19960402
APPLICATION INFO.:	US 1995-387038	19950210 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1993-134226, filed on 8 Oct 1993, now patented, Pat. No. US 5438042
DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Chan, Christina Y.
ASSISTANT EXAMINER: Degen, Nancy J.
LEGAL REPRESENTATIVE: Honor, Robert S.; Battle, Carl W.
NUMBER OF CLAIMS: 17
EXEMPLARY CLAIM: 1
LINE COUNT: 632
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

AB . . . component, 65-80% carbohydrate component and 16-25% protein component, based on total caloric content, wherein said protein comprises by weight 14-30% **glutamine** and 5-33% **arginine** and said composition has a nonprotein calorie to grams of nitrogen ratio of 150:1 to 80:1.

SUMM ISOCAL is an enteral formulation by Mead Johnson which utilizes casein and **soy** for its protein source, glucose oligosacchrides for its carbohydrate source and **soy** oil and medium chain **triglycerides** (**MCT**) oil for its lipid source.

SUMM OSMOLITE is manufactured by Ross and utilizes as its protein source casein and **soy**, corn starch for its carbohydrate source and fifty percent **MCT** oil, forty percent corn oil and ten percent **soy** oil for its lipid source.

SUMM ENSURE is manufactured by Ross and utilizes casein and **soy** for protein source, corn starch and sucrose for a carbohydrate source and corn oil for a lipid source.

SUMM SUSTACAL manufactured by Mead Johnson utilizes casein and **soy** for its protein source, corn syrup and sucrose for its carbohydrate source and **soy** oil for its lipid source.

SUMM ENSURE PLUS manufactured by Ross is a high protein, high calorie composition using **soy** and casein for its protein source, corn starch and glucose for its carbohydrate source and corn oil for its lipid. . .

SUMM . . . high density composition with 2.0 calories/ml. MAGNACAL utilizes casein for its protein source, corn syrup for its carbohydrate source and **soy** oil for its lipid source.

SUMM . . . by Mead Johnson utilizes casein for its protein source, corn syrup and sucrose for its carbohydrate source and 70 percent **soy** bean oil. and 30 percent **MCT** oil for its lipid source.

SUMM ISOTEIN HN is manufactured by Sandoz and utilizes lactalbumin for its protein source, maltodextrin for its carbohydrate source and **soy** oil and **MCT** oil for its lipid source.

SUMM VIVONEX T.E.N. is manufactured by Sandoz and comprises branched chain amino acids, **glutamine** and **arginine** as the protein source, safflower oil as the lipid source, and maltodextrin and modified

starch as the ca[redacted]hydrate source.

SUMM IMPACT is manufa[redacted]red by Sandoz and comprises **ar**[redacted]**ine** and caseinates as the protein source, maltodextrins as the carbohydrate, and

menhaden oil and structured lipids as the lipids source.

SUMM U.S. Pat. No. 4,752,618 describes a dietary supplement and method of minimizing infections therewith, comprising omega-3 and **omega-6** fatty acid such as safflower oil and menhaden oil.

SUMM U.S. Pat. No. 4,847,296 describes **triglyceride** preparations for enteral administration. to prevent catabolism and increase protein synthesis in subjects undergoing severe metabolic stress.

SUMM . . . describes enteral compositions for treating traumatic injury comprising an intact protein (from lactalbumin egg albumen or whey and the like), **arginine**, carbohydrate (glucose polymers, disaccharides, starches and the like), lipid comprising omega-3 fatty acids of fish oil, and necessary vitamins and. . .

SUMM U.S. Pat. No, 5,231,085 describes enteral compositions comprising **arginine**, **ornithine**, a nucleobase, omega-3 polyunsaturated fatty acids, and **omega-6** polyunsaturated fatty acids.

SUMM . . . from 16 to 25% protein component, said protein component comprising based on the free base 14 to 30% by weight **glutamine** and 5 to 33% by weight **arginine**, said **glutamine** and **arginine** being in free base form, ingestible salt form, partially hydrolyzed protein form or intact protein form,

SUMM . . . from 16 to 25% protein component, said protein component comprising based on the free base 14 to 30% by weight **glutamine** and 5 to 33% by weight **arginine**, said **glutamine** and **arginine** being in free base form, ingestible salt form, partially hydrolyzed protein form or intact protein form,

SUMM . . . the art, such as animal oils, fish oils, vegetable oils and synthetic lipids. Lipid sources include, for example, medium chain **triglycerides**, corn oil, soybean oil, peanut oil, olive oil, safflower oil, sunflower oil, cotton oil, canola oil and the like. The. . .

SUMM . . . 4 to 10% of long chain fatty acids having about 14-24 carbon atoms and 0 to 20% of medium chain **triglycerides** having fatty acid chains of about 6-12 carbon atoms.

SUMM The lipid component preferably comprises **omega-6** polyunsaturated fatty acids (i.e., linoleic acid) at 2-4% of total calories and omega-3 polyunsaturated fatty acids (i. e., linolenic acid). . .

SUMM . . . sources of intact protein, protein hydrolysates and crystalline amino acids used in enteral feeding compositions such as, for example, casein, **soy**, lactalbumin, egg albumen, whey and the like. The protein component of the claimed composition comprises based on free base 14 to 30% (preferably 22-23%) by weight **glutamine** and 5 to 33% (preferably 11-12%) by weight **arginine**. The **glutamine** and **arginine** can be in free base form, ingestible salt form, partially hydrolyzed protein form or intact protein form. Preferably, the composition comprises, based on total caloric content of the composition, **arginine** ranging from 1 to 6% based on the free base.

SUMM The composition of this invention has maintained its ratio of essential to nonessential amino acid even though **arginine** and **glutamine** have been added. This critical balance has been maintained through selected and careful calculations of each amino acid and has. . .

SUMM . . . from lactose, (which may be a problem in the critically ill due to lactose intolerance) and preferably contains no sucrose, **fructose** or dietary fiber.

SUMM **Arginine** is included in the compositions of this invention although it is classified as a nonessential amino acid. It is not considered to be an essential dietary constituent for humans in the

normal, unstress[redacted]human; the urea cycle provides [redacted]fficient **arginine** for maint[redacted]nce. However, endogenous biosy[redacted]esis of **arginine** may not be sufficient for maximal tissue regeneration or positive nitrogen balance in trauma or stress. Dietary **arginine** enrichment may diminish protein catabolism and hence, reduce urinary nitrogen excretion in trauma or stress and improve immune function.

SUMM The level of **arginine** in the preferred composition is about 1-6% (more preferably about 2%) of calories providing about 5 grams per liter. The **arginine** level is based on experiments (for example, using a third degree 30% body surface area burn model in guinea pigs). . . . containment as assessed by the size of the pustules after intradural staphylococcal injections. It has also been shown that plasma **arginine** concentrations had a high correlation with a number of parameters indicating resistance to infection, such as total protein, albumin, transferrin, C3 levels and opsonic index in severely burned children. Studies of surgical patients found that supplemental **arginine** significantly enhanced lymphocyte blastogeneses and increased CD4 phenotype (% T cells) postoperatively. The beneficial effect of **arginine** on the immune system appeared distinct from its more moderate effect on nitrogen balance.

SUMM **Glutamine** is utilized at a high rate by the intestinal cells in the basal state, while its uptake and metabolism increase even further in the course of catabolic illness. It has been proposed that **glutamine** deficiency may develop in the course of many catabolic diseases and that this deficiency may have an important impact on intestinal mucosal integrity and function. Increased uptake of **glutamine** by the gut in response to stress and critical illness spares glucose as an intestinal fuel.

SUMM Aside from **glutamine**'s role in the gut, there is some evidence of other benefits: spares glucose as an intestinal fuel; supports release of gluconeogenic precursors; provides a respiratory fuel for fibroblasts and lymphoid tissue. Patients who are at high risk of developing **glutamine** "deficiency" may benefit from the incorporation of **glutamine** at 14-30% by weight of the protein component of the enteral nutritional composition of this invention.

SUMM . . . daily requirement is unknown for mammalian species including humans. Carnitine is synthesized in the liver from the essential amino acids **lysine** and methionine. If the liver is impaired, it is possible that synthesis of carnitine may also be impaired. Since all.

SUMM

INGREDIENT	AMOUNT (WT. %)
MALTODEXTRIN	69.32
L-**GLUTAMINE**	3.773
MODIFIED FOOD STARCH	3.773
L-**LEUCINE**	2.547
L-**ARGININE** ACETATE	2.536
SOYBEAN OIL	2.505
MAGNESIUM GLUCONATE	1.729
L-**LYSINE** ACETATE	1.486
L-VALINE	1.273
L-ISOLEUCINE	1.273
CALCIUM GLYCEROPHOSPHATE	1.258
L-PHENYLALANINE	1.078
L-METHIONINE	0.9265
CITRIC ACID	0.7755
L-THREONINE	0.7114
POTASSIUM CHLORIDE	0.5450
L-TYROSINE	0.4569

L-HISTIDINE MONOHYDROCHLORIDE	0.[redacted]8
SODIUM CITRATE	0.4402
L-ASPARTIC ACID	0.4192
L-PROLINE	0.3878
POTASSIUM CITRATE	0.3668
SODIUM PHOSPHATE DIBASIC	0.2851
L-TRYPTOPHAN	0.2587
L-SERINE	0.2159
CHOLINE BITARTRATE	0.2154
L-**ALANINE**	0.1937
GLYCINE	0.1886
POTASSIUM SORBATE	0.1467
POLYGLYCEROL ESTERS OF F.A.	0.1308
TAURINE	0.08300
VITAMIN E ACETATE	0.05659
ASCORBIC ACID	0.05072
L-CARNITINE	0.04150
BIOTIN	0.01761
ZINC SULFATE	0.01572
FERROUS SULFATE	0.01404
NIACINAMIDE	0.01199

VITAMIN. . .

DETD

Ingredient	Wt. %
L-**glutamine**	20.6609
L-**leucine**	13.9461
L-**arginine** acetate	13.8887
L-**lysine** acetate	8.1381
L-isoleucine	6.9731
L-valine	6.9731
L-phenylalanine	5.9033
L-methionine	5.0734
L-threonine	3.8957
L-tyrosine	2.5023
L-histidine HCL	2.4793
L-aspartic acid	2.2957
L-proline	2.1235
L-tryptophan	1.4164
L-serine	1.1823
L-**alanine**	1.0606
glycine	1.0330
taurine	0.4545

CLM What is claimed is:

. . . acids in free base or ingestible salt form and comprises based on the free base 22% to 30% by weight **glutamine** and 11% to 33 by weight **arginine**, and at least 40% by weight essential amino acids, wherein said composition has a nonprotein calorie to grams of nitrogen. . .

. . . acids in free base or ingestible salt form and comprises, based on the free base, 22% to 23% by weight **glutamine** and 11% to 12% by weight **arginine** and at least 40% by weight essential amino acids, wherein said composition has a nonprotein calorie to grams of nitrogen. . .

. . . content of said composition, 4% to 10% of 14-24-carbon long chain fatty acids and 0 to 20% of medium chain **triglycerides** having fatty acid chains Of 6-12 carbon atoms.

. . . in free base form, ingestible salt form, partially hydrolyzed protein

form or intact p[redacted]ein form, 14% to 30% by weight **glutamine** and 5% to 33% by [redacted]ight **arginine**, based on the fr[redacted]base form, wherein said protein component contains an amino acid premix comprising about, based on total weight of said amino acid premix:

Ingredient	Wt. %
L-**glutamine**	20.6609
L-**leucine**	13.9461
L-**arginine** acetate	13.8887
L-**lysine** acetate	8.1381
L-isoleucine	6.9731
L-valine	6.9731
L-phenylalanine	5.9033
L-methionine	5.0734
L-threonine	3.8957
L-tyrosine	2.5023
L-histidine HCl	2.4793
L-aspartic acid	2.2957
L-proline	2.1235
L-tryptophan	1.4164
L-serine	1.1823
L-**alanine**	1.0606
glycine	1.0330
taurine	0.4545:

wherein said composition has a nonprotein calorie to grams of nitrogen ranging from 150:1 to 80:1; and wherein. . .

L19 ANSWER 2 OF 2 USPATFULL
ACCESSION NUMBER: 95:69268 USPATFULL
TITLE: Enteral nutritional composition having balanced amino acid profile
INVENTOR(S): Schmidl, Mary K., Arden Hills, MN, United States
Kvamme, Candis, Brooklyn Park, MN, United States
PATENT ASSIGNEE(S): Sandoz Nutrition Ltd., Berne, Switzerland (non-U.S. corporation)

	NUMBER	DATE
PATENT INFORMATION:	US 5438042	19950801
APPLICATION INFO.:	US 1993-134226	19931008 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Wityshyn, Michael G.
ASSISTANT EXAMINER: Degen, Nancy
LEGAL REPRESENTATIVE: Honor, Robert S.; Battle, Carl W.
NUMBER OF CLAIMS: 1
EXEMPLARY CLAIM: 1
LINE COUNT: 574
CAS INDEXING IS AVAILABLE FOR THIS PATENT.
AB . . . a protein component, based on total caloric content is disclosed. This protein component of this composition comprises, by weight, 14-30% **glutamine** and 5-33% **arginine**. The non-protein calorie to grams of nitrogen ratio ranges from 150:1 and 80:1.
SUMM ISOCAL is an enteral formulation by Mead Johnson which utilizes casein and **soy** for its protein source, glucose oligosacchrides for its carbohydrate source and **soy** oil and medium chain **triglycerides** (**MCT**) oil for its lipid source.
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SUMM U.S. Pat. No. 4,752,618 describes a dietary supplement and method of minimizing infections therewith, comprising omega-3 and **omega-6** fatty acid such as safflower oil and menhaden oil.

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SUMM The lipid component preferably comprises **omega-6** polyunsaturated fatty acids (i.e., linoleic acid) at 2-4% of total calories and omega-3 polyunsaturated fatty acids (i.e., linolenic acid) at. . .

SUMM . . . sources of intact protein, protein hydrolysates and crystalline amino acids used in enteral feeding compositions such as, for example,

casein, **soy**, lac[redacted]bumin, egg albumen, whey and th[redacted]like. The protein componen[redacted]f the claimed composition comp[redacted]es based on free base 14 to 30% (preferably 22-23%) by weight **glutamine** and 5 to 33% (preferably 11-12%) by weight **arginine**. The **glutamine** and **arginine** can be in free base form, ingestible salt form, partially hydrolyzed protein form or intact protein form. Preferably, the composition comprises, based on total caloric content of the composition, **arginine** ranging from 1 to 6% based on the free base.

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SUMM . . . from lactose, (which may be a problem in the critically ill due to lactose intolerance) and preferably contains no sucrose, **fructose** or dietary fiber.

SUMM **Arginine** is included in the compositions of this invention although it is classified as a nonessential amino acid. It is not considered to be an essential dietary constituent for humans in the normal, unstressed human; the urea cycle provides sufficient **arginine** for maintenance. However, endogenous biosynthesis of **arginine** may not be sufficient for maximal tissue regeneration or positive nitrogen balance in trauma or stress. Dietary **arginine** enrichment may diminish protein catabolism and hence, reduce urinary nitrogen excretion in trauma or stress and improve immune function.

SUMM The level of **arginine** in the preferred composition is about 1-6% (more preferably about 2%) of calories providing about 5 grams per liter. The **arginine** level is based on experiments (for example, using a third degree 30% body surface area burn model in guinea pigs) which demonstrated that diets containing about 2% **arginine** increased survival, improved delayed hypersensitivity as examined by dinitroflurobenzene, and heightened local bacterial containment as assessed by the size of the pustules after intradural staphylococcal injections. It has also been shown that plasma **arginine** concentrations had a high correlation with a number of parameters indicating resistance to infection, such as total protein, albumin, transferrin, C3 levels and opsonic index in severely burned children. Studies of surgical patients found that supplemental **arginine** significantly enhanced lymphocyte blastogeneses and increased CD4 phenotype (% T cells) postoperatively. The beneficial effect of **arginine** on the immune system appeared distinct from its more moderate effect on nitrogen balance.

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POTASSIUM CHLORIDE	0.5450
L-TYROSINE	0.4569
L-HISTIDINE MONOHYDROCHLORIDE	0.4528
SODIUM CITRATE	0.4402
L-ASPARTIC ACID	0.4192
L-PROLINE	0.3878
POTASSIUM CITRATE	0.3668
SODIUM PHOSPHATE DIBASIC	0.2851
L-TRYPTOPHAN	0.2587
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CHOLINE BITARTRATE	0.2154
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ASCORBIC ACID	0.05072
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ZINC SULFATE	0.01572
FERROUS SULFATE	0.01404
NIACINAMIDE	0.01199
VITAMIN. . .	

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L-threonine	3.8957
L-tyrosine	2.5023
L-histidine HCL	2.4793
L-aspartic acid	2.2957
L-proline	2.1235
L-tryptophan	1.4164
L-serine	1.1823

L-**alanine**	1.0606
glycine	1.0330
taurine	0.4545

CLM What is claimed is:

. . . grams of nitrogen ratio ranging from 150:1 to 80:1, and has the following formulation by solid weight:

Ingredient	Wt %
maltodextrin	69.32
L-**glutamine**	3.773
modified food starch	3.773
L-**leucine**	2.547
L-**arginine** acetate	2.536
soybean oil	2.505
magnesium gluconate	1.729
L-**lysine** acetate	1.486
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L-phenylalanine	1.078
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citric acid	0.7755
L-threonine	0.7114
potassium chloride	0.5450
L-tyrosine	0.4569
L-histidine monohydrochloride	0.4528
sodium citrate	0.4402
L-aspartic acid	0.4192
L-proline	0.3878
potassium citrate	0.3668
sodium phosphate dibasic	0.2851
L-tryptophan	0.2587
L-serine	0.2159
choline bitartrate	0.2154
L-**alanine**	0.1937
glycine	0.1886
potassium sorbate	0.1467
polyglycerol esters of fatty acids	0.1308
taurine	0.08300
vitamin E acetate	0.05659
ascorbic acid	0.05072
L-carnitine	0.04150
biotin	0.01761
zinc sulfate	0.01572
ferrous sulfate	0.01404
niacinamide. . .	

=> D IBIB 1-

YOU HAVE REQUESTED DATA FROM 2 ANSWERS - CONTINUE? Y/(N):Y

L9 ANSWER 4 OF 4 USPATFULL
ACCESSION NUMBER: 1998:57893 USPATFULL
TITLE: Composition of pyruvate and anti-cortisol compounds and
method for increasing protein concentration in a mammal
INVENTOR(S): Beale, Paxton K., 1801 Bush St., Suite 300, San Francisco, CA, United States 94109

	NUMBER	DATE
PATENT INFORMATION:	US 5756469	19980526
APPLICATION INFO.:	US 1996-686820	19960726 (8)

DOCUMENT TYPE: Utility
PRIMARY EXAMINER: Weddington, Kevin E.
LEGAL REPRESENTATIVE: Nickey, Donald O.Standley & Gilcrest
NUMBER OF CLAIMS: 14
EXEMPLARY CLAIM: 1
LINE COUNT: 542
CAS INDEXING IS AVAILABLE FOR THIS PATENT.

SUMM . . . treatment of rheumatoid arthritis. Thus, cortisol is a naturally occurring anti-inflammatory steroid. This catabolic hormone results in the release of **amino acids** from muscle tissue and prevents absorption of glucose. Cortisol, as a catabolic stress hormone, cannibalizes muscle tissue. High cortisol levels. . .

SUMM A further example of known cortisol blockers, the compound known as ipriflavone (7-isoproxy-**isoflavone**) is submitted. Ipriflavone is presently used in dosages of about 600 mgs per day to treat women suffering from osteoporosis.. . .

SUMM **Creatine** monohydrate is an additional cortisol blocker that, when combined with pyruvate, produces a synergistic effect in increasing the lean body mass of a mammal. The combination of pyruvate and **creatine** monohydrate also produces an increase in the athletic performance of the mammal by enhancing the energy level of the mammal.

SUMM . . . the use of pyruvate in enteral formulations, in combination with a cortisol blocker, such as phosphatidylserine, HMB, DHEA, CLA , **creatine** monohydrate, pregnenalone and the like, produces a synergistic effect in increasing the lean body mass or muscle tissue of a. . .

SUMM . . . thus, the water retention properties of the sodium salt are not beneficial. Pyruvate precursors in the form of pyruvamides or pyruvyl-**amino acids** are also useful in the present invention.
Pyruvyl-glycine is representative of the useful pyruvyl-**amino acids**. Another pyruvate precursor is pyruvyl-**creatine**.

SUMM . . . form of salts, for example, calcium pyruvate and magnesium pyruvate. U.S. Pat. Nos. 5,283,260 and 5,256,697 disclose uses for the pyruvyl-**amino acids** and methods for their production.

SUMM . . . disclosed a composition wherein the cortisol blocker is selected from the group consisting of phosphatidylserine, HMB, DHEA, CLA, anabolic steroids, **creatine** monohydrate, pregnenalone and Ipriflavone. Representative of the anabolic steroids useful in the present invention is androstenedione. Other forms of **creatine** such as **creatine-amino acid** adducts are also useful. Further, pyruvyl-**creatine** is a useful composition.

SUMM Specific forms of pyruvate useful in the present invention include magnesium pyruvate, calcium pyruvate, potassium pyruvate, pyruvyl-

creatine pyruvyl-glycine, pyruvamines, pyruvyl-alanine, pyruvyl-leucine, pyruvyl-valine, pyruvyl-isoleucine, pyruvyl-phenylalanine, pyruvyl-proline, pyruvyl-sarcosine, their amides, esters and salts, and mixtures thereof.

SUMM . . . calcium, potassium or magnesium pyruvate or mixtures thereof and at least one cortisol blocker selected from phosphatidylserine, HMB, DHEA, CLA, **creatine** monohydrate, pregnenalone, Ipriflavone, super physiological levels of leucine, anabolic steroids, such as androstenedione antioxidants, leucine metabolites, glutamic acid and its. . .

SUMM . . . from Lucas Meyer, Inc. of Decatur, Ill. in the form of powders or fluids. Corti-PS.TM. 30P is a specifically processed **soy** lecithin powder made especially for encapsulated, tabletted and powdered nutritional supplements. Corti-PS.TM. 30P has the following composition:

CLM What is claimed is:

. . . to claim 1 wherein said pyruvate is selected from the group comprising sodium pyruvate, calcium pyruvate, magnesium pyruvate, potassium pyruvate, pyruvyl-**creatine**, pyruvyl-glycine, pyruvamides, pyruvyl-alanine, pyruvyl-leucine, pyruvyl-valine, pyruvyl-isoleucine, pyruvyl-phenylalanine, pyruvyl-proline, pyruvyl-sarcosine, their amides, esters and salts and mixtures thereof.

. . . to claim 1 wherein said cortisol blocker is selected from the group consisting of phosphatidylserine, HMB, DHEA, CLA, anabolic steroids, **creatine** monohydrate, pregnenalone, Ipriflavone, super physiological levels of leucine, anabolic steroids, antioxidants, leucine metabolites, glutamic acid and its metabolites, glutamine and. . .

. . . claim 7 wherein said pyruvate is selected from the group comprising of sodium pyruvate, calcium pyruvate, magnesium pyruvate, potassium pyruvate, pyruvyl-**creatine**, pyruvyl-glycine, pyruvamides, pyruvyl-alanine, pyruvyl-leucine, pyruvyl-valine, pyruvyl-isoleucine, pyruvyl-phenylalanine, pyruvyl-proline, pyruvyl-sarcosine, their amides, esters and salts and mixtures thereof.

. . . to claim 7 wherein said cortisol blocker is selected from the group consisting of phosphatidylserine, HMB, DHEA, CLA, anabolic steroids, **creatine** monohydrate, pregnenalone, Ipriflavone, super physiological levels of leucine, anabolic steroids, antioxidants, leucine metabolites, glutamic acid and its metabolites, glutamine and. . .

L17 ANSWER 1 OF 1 USPATFULL

ACCESSION NUMBER: 1999:101404 USPATFULL

TITLE: Method for dispensing antioxidant vitamins by inhalation background of the invention

INVENTOR(S): Pera, Ivo E., P.O. Box 9224, Hollywood, FL, United States 33384

	NUMBER	DATE
PATENT INFORMATION:	US 5944012	19990831
APPLICATION INFO.:	US 1997-852331	19970507 (8)

RELATED APPLN. INFO.: Continuation of Ser. No. US 1996-621428, filed on 25 Mar 1996, now abandoned

DOCUMENT TYPE: Utility

PRIMARY EXAMINER: Weiss, John G.

ASSISTANT EXAMINER: Srivastava, V.

LEGAL REPRESENTATIVE: Malin, Haley, DiMaggio & Crosby

NUMBER OF CLAIMS: 13

EXEMPLARY CLAIM: 1

LINE COUNT: 571

AB A method is provided for dispensing dry powder antioxidant compounds, preferably consisting of vitamin C, vitamin E, betacarotene and a membrane permeation enhancer such as lactose. The compound is administered via a conventional dry powder inhaler to deliver said the compound into the subject's respiratory tract in order to enhance prophylactic and therapeutic effects of the antioxidant vitamins. Other antioxidant vitamins can also be included within the dry powder compound.

SUMM . . . of the tested, clinical population is allergic to corn starch and other corn products and about another 10 percent to **soy** products. These allergies can be sufficiently severe to produce very unpleasant symptoms when vitamin tablets using these fillers and binders. . .

DETD . . . art that various other antioxidants vitamins can be used without departing from the spirit of the invention. Such antioxidants comprise: **Coenzyme Q**-10 (**Ubiquinone**), SOD (Superoxide Dismutase), Catalase, GSH (Glutathhione Peroxidase), Selenium, **Alpha Lipoic Acid**, Pychogenol, etc., and rights to such alternatives are particularly reserved, especially those which fall within the scope of the appended. . .

AN 1978:131042 CAPLUS
DN 88:131042
TI Effect of lipoic acid on muscle strength and the working capacity of animals
AU Kolla, V. E.; Galetskii, G. I.; Ivanova, R. R.; Suslova, O. I.; Solomin, V. G.
CS USSR
SO Izuch. Biol. Deistviya Prod. Org. Sint. Prir. Soedin. (1976), 116-21. Editor(s): Pidemskii, E. L. Publisher: Permsk. Gos. Univ., Perm, USSR. CODEN: 37LRAS
DT Conference
LA Russian
CC 1-5 (Pharmacodynamics)
AB Lipoic acid [**57828-26-9**] (10-40 mg/kg) injected into mice increased work capacity (in a swimming test) and muscle strength. Lipoic acid prevented the effect of depolarizing and antidepolarizing muscle relaxant in healthy mice and in mice with toxic hepatitis.
ST lipoate muscle strength **exercise**
IT Muscle relaxants and Spasmolytics
(antagonist, lipoate)
IT **Exercise**
(lipoic acid effect on)
IT Muscle
(strength of, lipoic acid enhancement of)
IT **57828-26-9**
RL: BIOL (Biological study)
(muscle strength and work capacity enhancement by)

AN 1997:713407 CAPLUS
DN 128:259
TI Thioctic acid stimulates muscle ATP production in patients with type II diabetes and diabetic polyneuropathy
AU Tritschler, Hans J.; Barbiroli, Bruno; Medori, R.; Iotti, S.; Lodi, R.; Zaniol, P.
CS Medical Department, ASTA Medica AG, Frankfurt, Germany
SO Antioxid. Health Dis. (1997), 6(Lipoic Acid in Health and Disease), 393-406
CODEN: AHDIEQ
PB Dekker
DT Journal
LA English
CC 1-10 (Pharmacology)
AB We assessed in vivo, by phosphorus magnetic resonance spectroscopy, the effect of thioctic acid treatment on energy metab., rate of ATP prodn., and ion transport in the gastrocnemius muscles of patients affected with long-lasting type II diabetes and sensorimotor polyneuropathy. Patients were studied at rest, during in-magnet **exercise**, and during postexercise recovery prior to and after 40 days of treatment with oral lipoate. Lipoate treatment resulted in different degrees of symptomatic improvement in 80% of patients, no improvement in 10%, and worsening in 10%. At rest we found a low phosphorylation potential in 50% of patients, while 50% were within the normal range. Lipoate treatment did not affect magnetic resonance spectroscopy (MRS) data on resting muscle in any patient. All patients showed a deficient ability to perform work for comparable levels of metabolic activation. After thioctic acid treatment, 30% showed an amelioration of muscle performance during work for comparable levels of metabolic activation. All patients showed a defective recovery of PCr, Pi, and pH, thus showing a deficit of mitochondrial respiration and ion transport. Treatment with thioctic acid resulted in an increased rate of PCr recovery in 50% of patients, increased rate of Pi recovery in 40%, and increased rate of pH recovery in 70%. Our in vivo findings support the hypothesis that the pos. effect of lipoate treatment on mitochondrial oxidn., rate of ATP prodn., and ion transport is mainly due to increased availability of glucose inside the cell.
ST thioctic acid diabetes therapy
IT Antidiabetic agents
Diabetic neuropathy
Energy metabolism (animal)
Gastrocnemius muscle
Ion transport (biological)
Mitochondrial respiration
Muscle
Non-insulin-dependent diabetes mellitus
Phosphorylation (biological)
(thioctic acid stimulates muscle ATP prodn. and glucose utilization in patients with type II diabetes and diabetic polyneuropathy)
IT **1077-28-7**, Thioctic acid
RL: BAC (Biological activity or effector, except adverse); THU

(Therapeutic use); BIOL (Biological study); USES (Uses)
(thioctic acid stimulates muscle ATP prodn. and glucose utilization in patients with type II diabetes and diabetic polyneuropathy)

IT 56-65-5, 5'-ATP, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(thioctic acid stimulates muscle ATP prodn. and glucose utilization in patients with type II diabetes and diabetic polyneuropathy)

IT 50-99-7, D-Glucose, biological studies
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(utilization; thioctic acid stimulates muscle ATP prodn. and glucose utilization in patients with type II diabetes and diabetic polyneuropathy)

AN 1998:699677 CAPLUS
DN 130:37674
TI Skeletal muscle and liver lipoyllysine content in response to exercise, training and dietary .alpha.-lipoic acid supplementation
AU Khanna, Savita; Atalay, Mustafa; Lodge, John K.; Laaksonen, David E.; Roy, Sashwati; Hanninen, Osmo; Packer, Lester; Sen, Chandan K.
CS Department of Physiology, University of Kuopio, Kuopio, 70211, Finland
SO Biochem. Mol. Biol. Int. (1998), 46(2), 297-306
CODEN: BMBIES; ISSN: 1039-9712
PB Academic Press
DT Journal
LA English
CC 18-2 (Animal Nutrition)
AB In human cells, .alpha.-lipoic acid (LA) is present in a lipoyllysine form bound in mitochondrial proteins that play a central role in oxidative metab. The effects of oral LA supplementation, single-bout strenuous exercise, and **endurance** exercise training on the lipoyllysine content in skeletal muscle and liver tissues were studied in rats. Incorporation of the lipoyl moiety into tissue proteins was not increased by increased dietary intake of LA. **Endurance** exercise training markedly increased the lipoyllysine content in the liver at rest. A bout of exhaustive exercise also increased the hepatic lipoyllysine content. A significant interaction of exhaustive exercise and training in the increase of tissue lipoyllysine content was evident. In the vastus lateralis skeletal muscle, the training did not influence the tissue lipoyllysine content, but a single bout of exhaustive exercise clearly increased the lipoyllysine level. Comparison of data on tissue lipoyllysine and free or loosely-bound LA showed lack of assocn. between these 2 parameters. The tightly protein-bound lipoyllysine pool in tissues appeared to be independent of the loosely-bound or free LA pool in the tissue. (c) 1998 Academic Press.
ST nutrition lipoate muscle liver lipoyllysine exercise training
IT Exercise
Liver
Muscle
Nutrition (animal)
(dietary .alpha.-lipoic acid, exercise and training effects on protein lipoyllysine in skeletal muscles and liver of rats)
IT 1676-89-7
RL: BPR (Biological process); BIOL (Biological study); PROC (Process)
(dietary .alpha.-lipoic acid, exercise and training effects on protein lipoyllysine in skeletal muscles and liver of rats)
IT **1200-22-2**, .alpha. Lipoic acid
RL: BPR (Biological process); FFD (Food or feed use); BIOL (Biological study); PROC (Process); USES (Uses)
(dietary .alpha.-lipoic acid, exercise and training effects on protein lipoyllysine in skeletal muscles and liver of rats)
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RE
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AN 1975:153249 CAPLUS
DN 82:153249
TI Arterial enzymes and their relation to atherosclerosis in pigeons
AU Zemplenyi, Tibor; Rosenstein, Alan J.
CS Sch. Med., Univ. South. California, Los Angeles, Calif., USA
SO Exp. Mol. Pathol. (1975), 22(2), 225-41
CODEN: EXMPA6
DT Journal
LA English
CC 14-3 (Mammalian Pathological Biochemistry)
AB Comparison of metabolic processes between the atherosclerosis-resistant Show Racer (R) and susceptible White Carnsau (S) pigeon strains was used for study of the factors which may predispose to atherosclerosis. In 4-6-year-old pigeons, the activity of lipoamide dehydrogenase and malate dehydrogenase was significantly lower in S than R arteries. The differences were not the result of aging or atherosclerosis, because they were also detected in arteries of young pigeons. Furthermore, the arteries of the young pigeons revealed a significantly higher activity of phosphofructokinase and aldolase in the arteries as compared with R arteries. The differences between the 2 strains are apparently inherited.

The low activity of lipoamide and malate dehydrogenases may slow the Krebs cycle and lead to low citrate and ATP prodn. The latter factor is an essential part of the feedback control adjustments that regulate the efficiency of glycolysis via phosphofructokinase. Increased dependence of the S arteries on glycolysis appears to facilitate the development of atherosclerosis in these birds, and the mechanism may be similar to the mechanism by which tissue hypoxia induces lipid accumulation and connective tissue alterations in the arterial wall. Higher activities in female than male arteries of phosphofructokinase, aldolase, isocitrate dehydrogenase, glycerokinase, ATPase and creatine phosphokinase were also obsd.
ST atherosclerosis artery enzyme sex; lipoamide dehydrogenase artery atherosclerosis; malate dehydrogenase artery atherosclerosis
IT Atherosclerosis
(enzymes of artery in, of pigeon)
IT Pigeon
(enzymes of artery of, in atherosclerosis)
IT Artery, composition
(enzymes of, of pigeon in atherosclerosis)
IT 9001-18-7 9001-64-3 9001-80-3 9024-52-6
RL: BIOL (Biological study)
(of pigeon artery, in atherosclerosis)

AN 132:83671 CAPLUS
TI Creatine-containing formulations
IN Seyerl, Joachim
PA SKW Trostberg A.-G., Germany
SO Ger. Offen., 6 pp.
CODEN: GWXXBX
DT Patent
LA German
IC ICM A61K031-195
CC 63-6 (Pharmaceuticals)
Section cross-reference(s): 17
FAN.CNT 1

PATENT NO.	KIND	DATE	APPLICATION NO.	DATE
DE 19830768	A1	20000113	DE 1998-19830768	19980709

AB Pharmaceutical formulations for treatment of muscular dystrophy and other myopathies, as well as nutritional supplements, are provided which contain creatine or a salt thereof 0.1-10 g, .gtoreq.1 neurotransmitter or precursor thereof 2 mg-8 g, .alpha.-lipoic acid 0.3-3 g, and optionally L-carnitine or a salt thereof 0.8-1 g and/or coenzyme Q10 50-150 mg (all amts. refer to daily doses). Creatine contributes to muscle energy metab. through its conversion to phosphocreatine. Neurotransmitters and assocd. compds. such as choline and taurine improve nerve and muscle function; hypericin, an MAO inhibitor, functions as an antidepressant. .alpha.-Lipoic acid and L-carnitine act as hypolipemic agents. The formulations synergistically improve muscle strength and efficiency in patients with muscular dystrophy or atrophy without side effects. Thus, a medicinal tea contained creatine pyruvate 5000, carnitine 500, taurine 500, choline 500, .alpha.-lipoic acid 500, St. John's wort ext. (contg. 0.3 wt.% hypericin) 300, and sucrose 200 mg.
ST muscular dystrophy creatine neurotransmitter lipoate; atrophy muscular carnitine coenzyme Q10; choline muscular dystrophy
IT Muscle, disease
Muscular dystrophy
St.-John's-wort (Hypericum perforatum)
(creatine-contg. formulations)
IT Neurotransmitters
RL: BAC (Biological activity or effector, except adverse); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(creatine-contg. formulations)
IT Drug interactions
(synergistic; creatine-contg. formulations)
IT 57-00-1, Creatine 60-18-4, L-Tyrosine, biological studies 62-49-7 107-35-7, Taurine 303-98-0, Coenzyme Q10 541-15-1, L-Carnitine 548-04-9, Hypericin 1200-22-2, .alpha.-Lipoic acid 4350-09-8 6645-46-1, L-Carnitine hydrochloride 36687-82-8, L-Carnitine tartrate 208535-04-0 220349-64-4, L-Carnitine fumarate, biological studies 253786-77-5, biological studies
RL: BAC (Biological activity or effector, except adverse); FFD (Food or feed use); THU (Therapeutic use); BIOL (Biological study); USES (Uses)
(creatine-contg. formulations)

AN 1994:315465 CAPLUS
DN 120:315465
TI Protective effect of lipoic acid on biphasic creatine kinase release from rat heart in early ischemia reperfusion period
AU Gao, Tianli; Zhang, Ying
CS Dep. Biol., Peking Univ., Beijing, Peop. Rep. China
SO Beijing Daxue Xuebao, Ziran Kexueban (1993), 29(4), 492-7
CODEN: PCTHAP; ISSN: 0479-8023
DT Journal
LA Chinese
CC 1-8 (Pharmacology)
AB Ischemia reperfusion injury of heart induces massive release of creatine kinase (CK). By means of Langendorff method isolated rat heart was perfused with Krebs-Henseleit (K-H) soln. The perfused sequence was 10 min equil., 10 min global ischemia, and 3 min reperfusion. Effluents were collected every 15 s for CK activity (U/L) anal. as an index of cellular damage to investigate the protective effect of lipoic acid on reperfusion injury. Perfusion without substrate caused a biphasic CK release which could be reduced or deleted by inclusion of lipoic acid (LA, 3,5 .times. 10-5 mol/L) or glucose (11 mmol/L) to the perfusate. Inclusion of LA before and after ischemia could similarly decrease total CK release and the 1st peak, as well as delete the 2nd peak. Glucose plus LA had additively protective effect to CK release. LA treatment also decreased the incidence of arrhythmia during 3 min reperfusion period. In all LA treated groups the redn. of CK release by LA may be attributed to its free radical scavenger mechanism.
ST lipoate creatine kinase heart ischemia reperfusion
IT Radicals, biological studies
RL: BIOL (Biological study)
(scavenger, lipoic acid as, biphasic creatine kinase release from heart in early ischemia reperfusion period protection by)
IT Heart, disease
(ischemia, reperfusion period, biphasic creatine kinase release in early, lipoic acid protection of)
IT Perfusion
(re-, period from heart ischemia, biphasic creatine kinase release in early, lipoic acid protection of)
IT 57828-26-9, Lipoic acid
RL: BIOL (Biological study)
(biphasic creatine kinase release from heart in early ischemia reperfusion period protection by)
IT 9001-15-4, Creatine kinase
RL: BIOL (Biological study)
(biphasic release from heart in early ischemia reperfusion period, lipoic acid protection of)